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L2: Entry 61 of 86 File: USPT Sep 24, 1996

DOCUMENT-IDENTIFIER: US RE35338 E
TITLE: Sustained release delivery of water soluble bio-molecules and drugs using phosphokipid-coated microcrystals, microdroplets and high-concentration lipsomes

Brief Summary Paragraph Right (6):
Liposomes, aqueous core vesicles formed from membrane-forming phospholipids such as lecithin, were first described by Bangham, Standish & Watkins (in J. Mol. Biol. 13:238, 1965). Liposomes produced by homogenization are multi-lamellar, with concentric bilayer membranes. Liposomes produced by sonication are small and unilamellar phospholipid vesicles as described by Haung (in Biochem. 8:344, 1969). Liposomes have the ability to entrap polar and highly-charged molecules in their aqueous interiors. Publications describing the use of liposomes to entrap and deliver water-soluble drugs appeared in the early and mid-1970's (cf. Gregoriadis: "The Carrier Potential of Liposomes in Biology and Medicine38 , New. England Journal of Medicine 295:704-710, 1976) A large number of patents have been granted for entrapment of water-soluble drugs and proteins (Papahadjopoulos, U.S. Pat. No. 4,078,052, 1978; Schneider, U.S. Pat. No. 4,089,801, 1978; Miller & Djordjevich, U.S. Pat. No. 4,133,874, 1979; Papahadjopoulos et al., U.S. Pat. No. 4,235,871, 1980; Weber et al. U.S. Pat. No. 4,38,052, 1984; Deamer, U.S. Pat. No. 4,515,736, 1985; Jizomoto, U.S. Pat. No. 4,762,720, 1988; Farmer & Beissinger, U.S. Pat. No. 4,776,991, 1988; Yagi et al., U.S. Pat. No. 4,756,910, 1988; Lenk et al., U.S. Pat. No. 5,030,453 are a small fraction of the available examples). However, most of these liposome inventions rely on complicated methods of preparation, including dissolution in organic solvents and evaporation, treatment with detergents and the like. Furthermore, the intra-vesicular space as described in these publications is always less than 10% of the total aqueous space. Thus the "stability of the entrapment" is a serious consideration since slow permeation of the entrapped molecules while the preparation is on the shelf will result in 90% of the molecules eventually being outside of the liposomes, with loss or the intended benefit of the encapsulation.

Brief Summary Paragraph Right (54):
CLASS D: Cholesterol and steroids. These can ont be used as a sole coating material: They do not form membranes in the pure state. They can be added to the lecithin or other coating material to change its surface activity, the "microviscosity" or distensibility of the coating. With a steroid hormone (estrogen, androgen, mineralo- or glucocorticoid), it is possible to influence the local tissue response to the microcrystals as well as influencing their physical disposition.

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L2: Entry 63 of 86 File: USPT Nov 28, 1995

DOCUMENT-IDENTIFIER: US 5469854 A
TITLE: Methods of preparing gas-filled liposomes

Detailed Description Paragraph Right (96):
Other suitable therapeutics include, but are not limited to: antineoplastic agents, such as platinum compounds (e.g., spiroplatin, cisplatin, and carboplatin), methotrexate, adriamycin, taxol, mitomycin, ansamitocin, bleomycin, cytosine arabinoside, arabinosyl adenine, mercaptopolylysine, vincristine, busulfan, chlorambucil, melphalan (e.g., PAM, L-PAM or phenylalanine mustard), mercaptopurine, mitotane, procarbazine hydrochloride dactinomycin (actinomycin D), daunorubicin hydrochloride, doxorubicin hydrochloride, mitomycin, plicamycin (mithramycin), aminoglutethimide, estramustine phosphate sodium, flutamide, leuprolide acetate, megestrol acetate, tamoxifen citrate, testolactone, trilostane, amsacrine (m-AMSA), asparaginase (L-asparaginase) Erwina asparaginase, etoposide (VP-16), interferon .alpha.-2a, interferon .alpha.-2b, teniposide (VM-26), vinblastine sulfate (VLB), vincristine sulfate, bleomycin, bleomycin sulfate, methotrexate, adriamycin, and arabinosyl; blood products such as parenteral iron, hemin, hematoporphyrins and their derivatives; biological response modifiers such as muramyldipeptide, muramyltripeptide, microbial cell wall components, lymphokines (e.g., bacterial endotoxin such as lipopolysaccharide, macrophage activation factor), sub-units of bacteria (such as Mycobacteria, Corynebacteria), the synthetic dipeptide N-acetyl-muramyl-L-alanyl-D-isoglutamine; anti-fungal agents such as ketoconazole, nystatin, griseofulvin, flucytosine (5-fc), miconazole, amphotericin B, ricin, and .beta.-lactam antibiotics (e.g., sulfazecin); hormones such as growth hormone, melanocyte stimulating hormone, estradiol, beclomethasone dipropionate, betamethasone, betamethasone acetate and betamethasone sodium phosphate, vetamethasone disodium phosphate, vetamethasone sodium phosphate, cortisone acetate, dexamethasone, dexamethasone acetate, dexamethasone sodium phosphate, flunsolide, hydrocortisone, hydrocortisone acetate, hydrocortisone cypionate, hydrocortisone sodium phosphate, hydrocortisone sodium succinate, methylprednisolone, methylprednisolone acetate, methylprednisolone sodium succinate, paramethasone acetate, prednisolone, prednisolone acetate, prednisolone sodium phosphate, prednisolone tebutate, prednisone, triamcinolone, triamcinolone acetonide, triamcinolone diacetate, triamcinolone hexacetonide and fludrocortisone acetate; vitamins such as cyanocobalamin neinoic acid, retinoids and derivatives such as retinol palmitate, and .alpha.-tocopherol; peptides, such as manganese super oxide dimutase; enzymes such as alkaline phosphatase; anti-allergic agents such as amelexanox; anti-coagulation agents such as phenprocoumon and heparin; circulatory drugs such as propranolol; metabolic potentiators such as glutathione; antituberculars such as para-aminosalicylic acid, isoniazid, capreomycin sulfate cycloserine, ethambutol hydrochloride ethionamide, pyrazinamide, rifampin, and streptomycin sulfate; antivirals such as acyclovir, amantadine azidothymidine (AZT or Zidovudine), ribavirin and vidarabine monohydrate (adenine arabinoside, ara-A); antianginals such as diltiazem, nifedipine, verapamil, erythrityl tetranitrate, isosorbide dinitrate, nitroglycerin (glyceryl trinitrate) and pentaerythritol tetranitrate; anticoagulants such as phenprocoumon, heparin; antibiotics such as dapsone, chloramphenicol, neomycin, cefaclor, cefadroxil, cephalexin, cephradine erythromycin, clindamycin, lincomycin, amoxicillin, ampicillin, bacampicillin, carbenicillin, dicloxacillin, cyclacillin, picloxacillin, hetacillin, methicillin, nafcillin, oxacillin, penicillin G, penicillin V, ticarcillin rifampin and tetracycline; antiinflammatories such as difunisal, ibuprofen, indomethacin, meclofenamate, mefenamic acid, naproxen, oxyphenbutazone, phenylbutazone, piroxicam,

sulindac, tolmetin, aspirin and salicylates; antiprotozoans such as chloroquine, hydroxychloroquine, metronidazole, quinine and meglumine antimonate; antirheumatics such as penicillamine; narcotics such as paregoric; opiates such as codeine, heroin, methadone, morphine and opium; cardiac glycosides such as deslanoside, digitoxin, digoxin, digitalin and digitalis; neuromuscular blockers such as atracurium besylate, gallamine triethiodide, hexafluorenium bromide, metocurine iodide, pancuronium bromide, succinylcholine chloride (suxamethonium chloride), tubocurarine chloride and vecuronium bromide; sedatives (hypnotics) such as amobarbital, amobarbital sodium, aprobarbital, butabarbital sodium, chloral hydrate, ethchlorvynol, ethinamate, flurazepam hydrochloride, glutethimide, methotrimeprazine hydrochloride, methyprylon, midazolam hydrochloride, paraldehyde, pentobarbital, pentobarbital sodium, phenobarbital sodium, secobarbital sodium, talbutal, temazepam and triazolam; local anesthetics such as bupivacaine hydrochloride, chloroprocaine hydrochloride, etidocaine hydrochloride, lidocaine hydrochloride, mepivacaine hydrochloride, procaine hydrochloride and tetracaine hydrochloride; general anesthetics such as droperidol, etomidate, fentanyl citrate with droperidol, ketamine hydrochloride, methohexital sodium and thiopental sodium; and radioactive particles or ions such as strontium, iodide rhenium and yttrium.

Detailed Description Paragraph Right (113):
The liposomes may also be designed so that there is a symmetric or an asymmetric distribution of the drug both inside and outside of the liposome.

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L2: Entry 72 of 86 File: USPT Mar 2, 1993

DOCUMENT-IDENTIFIER: US 5190761 A
TITLE: Electromagnetic field triggered drug and chemical delivery via liposomes

Detailed Description Paragraph Right (29):
Alternatively, the REVs or MLVs preparations can be treated to produce small unilamellar vesicles (SUVs), large unilamellar vesicles (LUVs) or oligolamellar vesicles (OLVs) which are characterized by sizes in the 0.04-0.08 .mu., 0.1-0.5 .mu., and mixed micron range, respectively. Because of the small particle sizes, SUVs suspensions can be optically quite clear, and thus advantageous and preferred for such applications as the delivery of steroid to the minuscule lung alveoli. Another advantage of SUVs, is the greater packing density of liposomes at a mucosal surface which can be achieved with smaller liposome particles, thus making SUVs preferred for inhalation, for treatment of deep lung diseases, degenerative interstitial pneumonia or in general for the intraveneous administration since the SUVs would get into the smallest peripheral veins and arteries.

Detailed Description Paragraph Right (75):
The role of oxygen and antioxidants was further investigated by modifying the DPPC:DPPG liposomes with antioxidant agents: .alpha.-tocopherol (Vitamin E) was incorporated at 2% mole fraction into the liposome membrane; and ascorbate (Vitamin C) was loaded at 35 mM into the interior aqueous compartment of the liposome. FIG. 16 depicts the data from microwave treatment experiments in which exposures were performed at 6 mW/gm for 15 minutes at the temperatures shown. The drug release data for the sham-exposed, control liposomes are consistent with the sham data for DPPC:DPPG liposomes shown hereinabove; a Tc is evident at about 39.degree.-40.degree. C. where drug release occurs spontaneously. Thus, modification of these liposomes with either of these antioxidant agents does not influence the liposome's ability to release drugs. When these liposomes are treated with microwaves both the ascorbate-modified and the .alpha.-tocopherol-modified liposomes exhibit increased drug release at temperatures below Tc, where the liposome is in the solid state. Interestingly, a comparison between modified and unmodified liposomes reveals that the microwave field increases drug release greatest for the unmodified liposomes (no antioxidants present). Thus, the protective effect of antioxidants seen in FIG. 15 with the antioxidants in the buffer outside the liposome, is also seen here with the antioxidant agent present in the liposome membrane and in the liposome interior.

L2: Entry 74 of 86 File: USPT Dec 8, 1992

DOCUMENT-IDENTIFIER: US 5169637 A
TITLE: Stable plurilamellar vesicles

Brief Summary Paragraph Right (7):
Liposomes which entrap a variety of compounds can be prepared, however, stability of the liposomes during storage is invariably limited. This loss in stability results in leakage of the entrapped aqueous soluble compound from the liposomes into the surrounding media, and can also result in contamination of the liposome contents by permeation of materials from the surrounding media into the liposome itself. As a result the storage life of traditional liposomes is very limited. Attempts to improve stability involved incorporating into the liposome membrane certain substances (hereinafter called "stabilizers") which affect the physical properties of the lipid bilayers (e.g., steroid groups). However, many of these substances are relatively expensive and the production of such liposomes is not cost-effective.

Detailed Description Paragraph Right (14):
Specific examples of suitable lipids useful in the production of SPLVs are phospholipids which include the natural lecithins (e.g., egg lecithin or soybean lecithin) and synthetic lecithins, such as saturated synthetic lecithins (e.g., dimyristoylphosphatidylcholine, or dipalmitoylphosphatidylcholine or distearoylphosphatidylcholine) and unsaturated synthetic lecithins (e.g., dioloyl-phosphatidylcholine or dilinoloylphosphatidylcholine. The SPLV bilayers can contain a steroid component such as cholesterol, coprostanol, cholestanol, cholestane and the like. When using compounds with acidic hydrophilic groups (phosphato, sulfato, etc.) the obtained SPLVs will be anionic; with basic groups such as amino, cationic liposomes will be obtained; and with polyethylenoxy or glycol groups neutral liposomes will be obtained. The size of the SPLVs varies widely. The range extends from about 100 nm to about 10,000 nm (10 microns) and usually about 100 nm to about 1500 nm.

Detailed Description Paragraph Right (34):
In the following experiments vesicles were prepared which contained radioactive tracer molecules within the occluded aqueous compartments. When placed in a buffer containing isotonic saline at neutral pH, SPLVs containing antibiotic exhibit prolonged stability in storage. The vesicles were prepared, each containing one of the following radio-labeled drugs: .sup.125 I-p-hydroxypropionic acid-derived gentamicin sulfate, .sup.14 C-indomethacin, and .sup.3 H-inulin. After storage at various temperatures for 14 days the vesicles were separated from the medium by centrifugation, and the relative amount of radioactivity that escaped from the vesicles into the medium was determined. The results demonstrated that SPLVs were more stable during storage than were MLVs.

Detailed Description Paragraph Right (79):
Experiments demonstrated that the salt concentration gradient across the liposomes, as opposed to the amount of the entrapped salt, is important in affecting the LSS. For example, FIG. 9 shows that if SPLVs were prepared in 0.145M salt (i.e., physiological concentration), but suspended in 0.290M salt, the resulting LSS resembles that of MLVs. Thus it appeared that a MLV-like LSS resulted if an osmotic gradient was imposed on SPLVs by increasing the salt concentration outside the liposomes (i.e., by exposing the SPLVs to a hypertonic environment). The LSS typical of SPLVs could similarly be achieved by suspending MLVs in a solution of low salt concentration (i.e., by exposing the MLVs to a hypotonic environment). FIG. 10

demonstrates, indeed, that MLVs prepared in 0.145M salt but suspended in 0.073M salt exhibit a SPLV-like LSS. The fact that the salt gradient is important is also seen in FIG. 11, which shows the LSS of MLVs prepared with 0.435M salt and then suspended in 0.145M salt; the LSS is again seen to be typical of that of that of SPLVs.

Detailed Description Paragraph Right (83):
It should be noted that a SPLV-like LSS resulted if SPLVs were either prepared with no osmotic stress (FIG. 14) or with solutions which were somewhat more concentrated than the buffer outside the liposome. The latter statement follows from the fact that the 0.145M salt used to prepare SPLVs lost about 10% of its water when the ether was evaporated during the SPLV formation process, thereby concentrating solutes.

Detailed Description Paragraph Table (3):
TABLE III COMPARISON OF MLVS AND SPLVS % Available Material Entrapped.sup.a Monophasic Emulsification Solvent System Encapsulation of: MLVs Method Method.sup.b bovine serum 15 20-50 .sup. ND.sup.c inulin (aqueous 2-6 20-37 37 space marker) albumin streptomycin 12-15 20-40 ND polyvinylpyrrolidone 5 25-35 ND (aqueous space) .sup.125 I-Gentamicin ND 33 38 .sup.14 C-Indomethacin ND 22 15 .sup.a Values are expressed as percent entrapped meaning the proportion o radioactive material in the liposome pellet (cpm) relative to the starting amount (cpm) added to the preparation. .sup.b Radiolabeled material to be entrapped was added to the monophase. After evaporation to a film and resuspension with aqueous buffer to form SPLVs, the preparation was pelleted and the radioactivity of the supernatant was determined. .sup.c Not determined.

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Search Results - Record(s) 1 through 18 of 18 returned.

1. Document ID: US 6368618 B1

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | Claims | KWIC | Draw Desc | Image

2. Document ID: US 6355666 B1

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | Claims | KWIC | Draw Desc | Image

3. Document ID: US 6306838 B1

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | Claims | KWIC | Draw Desc | Image

4. Document ID: US 6258378 B1

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5. Document ID: US 6028054 A

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6. Document ID: US 6004927 A

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☐ 7. Document ID: US 5939096 A

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | Claims | KWIC
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☐ 8. Document ID: US 5759566 A

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | Claims | KWIC
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☐ 9. Document ID: US 5747533 A

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | Claims | KWIC
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☐ 10. Document ID: US 5731346 A

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | Claims | KWIC
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☐ 11. Document ID: US 5585109 A

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | Claims | KWIC
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☐ 12. Document ID: US 5567592 A

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | Claims | KWIC
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☐ 13. Document ID: US 5356633 A

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | Claims | KWIC
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☐ 14. Document ID: US 4937254 A

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | Claims | KWIC
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☐ 15. Document ID: JP 11504930 W, WO 9635429 A1, DE 19518221 A1, NO 9705127 A, EP 831840 A1, US 5874422 A

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | Claims | KWIC
Draw. Desc | Image

☐ 16. Document ID: IL 118162 A, WO 9635414 A1, ZA 9603584 A, AU 9658119 A, EP 835103 A1, JP 11504638 W

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | Claims | KWIC
Draw. Desc | Image

☐ 17. Document ID: WO 9209268 A1, AU 664359 B, AU 9191279 A, EP 560900 A1, JP 06507882 W, EP 560900 B1, DE 69107309 E, US 5411743 A, ES 2071481 T3

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | Claims | KWIC
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☐ 18. Document ID: US 5036097 A, WO 9113618 A, AU 9174895 A, EP 518951 A1, JP 05506214 W, ES 2044829 T1, EP 496796 B1, AU 653921 B, ES 2044829 T3, AU 658139 B, US 35112 E, US 35213 E, JP 09025263 A, JP 2620413 B2, CA 2077653 C, JP 2816326 B2, JP 10259128 A, JP 10259178 A, AU 9883102 A, KR 9608230 B1, AU 710341 B, AU 710342 B, CA 2069961 C

Terms	Documents
(liposome$) same (NSAID$)	18

WEST Search History

DATE: Wednesday, April 17, 2002

Set Name side by side	Query	Hit Count	Set Name result set
DB=USPT,JPAB,EPAB,DWPI,TDBD; PLUR=YES; OP=OR			
L8	(liposome$) same (NSAID$)	18	L8
L7	(liposome$) same (outside adj10 NSAID$)	0	L7
L6	(liposome$) same (outside adj5 NSAID$)	0	L6
L5	(liposome$) same (outside adj2 NSAID$)	0	L5
L4	(liposome$) same (outside adj2 drug$)	5	L4
L3	(liposome$) same outside adj2 (steroid$ or indomethacin or aspirin)	0	L3
L2	L1 and (steroid$ or indomethacin or aspirin)	86	L2
L1	outside adj2 liposome$	212	L1

END OF SEARCH HISTORY

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Search Results - Record(s) 1 through 2 of 2 returned.

☐ 1. Document ID: US 5190766 A

L1: Entry 1 of 2 File: USPT Mar 2, 1993

US-PAT-NO: 5190766
DOCUMENT-IDENTIFIER: US 5190766 A

TITLE: Method of controlling drug release by resonant sound wave

DATE-ISSUED: March 2, 1993

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Ishihara; Ken	Chigusa, Takarazuka-shi, Hyogo			JPX

US-CL-CURRENT: 424/489; 424/491, 424/493, 424/499, 604/22

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | KWIC | Draw. Desc | Image

☐ 2. Document ID: EP 274174 A, AU 8767559 A, DE 3782492 G, DK 8700297 A, EP 274174 B1, JP 01042418 A, JP 63258423 A, NO 8700299 A, US 4797285 A

L1: Entry 2 of 2 File: DWPI Jul 13, 1988

DERWENT-ACC-NO: 1988-191810
DERWENT-WEEK: 198828

TITLE: Liposome-anthraquinone drug compsn. - contg. a lipophilic free-radical scavenger and a tri:hydroxamic acid chelating agent for increased stability

INVENTOR: BARENHOLZ, Y; GABIZON, A

PRIORITY-DATA: 1987EP-0300213 (January 9, 1987), 1987JP-0018142 (January 27, 1987), 1985US-0806084 (December 6, 1985)

PATENT-FAMILY:

PUB-NO	PUB-DATE	LANGUAGE	PAGES	MAIN-IPC
EP 274174 A	July 13, 1988	E	029	
AU 8767559 A	July 21, 1988		000	
DE 3782492 G	December 10, 1992		000	A61K009/50
DK 8700297 A	July 21, 1988		000	
EP 274174 B1	November 4, 1992	E	027	A61K009/50
JP 01042418 A	February 14, 1989		000	
JP 63258423 A	October 25, 1988		000	
NO 8700299 A	August 15, 1988		000	
US 4797285 A	January 10, 1989		016	

INT-CL (IPC): A61J 5/00; A61K 9/50; A61K 31/70; A61K 37/22; B01J 13/02; B23B 5/16

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | KWIC | Draw. Desc | Image

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Terms	Documents
liposome$ same (drug adj1 outside)	2

Display Format: - Change Format

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L7: Entry 17 of 36 File: USPT May 11, 1993

DOCUMENT-IDENTIFIER: US 5210073 A
TITLE: Method for treating cancer therapy radiation damage or arteriosclerosis using human ADF

Brief Summary Paragraph Right (10):
Superoxide dismutase (SOD) has an activity of scavenging O.sub.2.sup.- which is a free radical. Investigations are now under way to develop SOD as an antiinflammatory agent. However, its half-life in the body is very short, within 10 minutes, so that it is necessary to make a device by chemical modification or containment in liposomes, etc., in order to prolong the half-life. Such requirements result in problems in clinical applications of SOD.

L7: Entry 16 of 36 File: USPT Oct 18, 1994

DOCUMENT-IDENTIFIER: US 5356633 A
TITLE: Method of treatment of inflamed tissues

Brief Summary Paragraph Right (59):
In a related embodiment, for use in treating a psoriatic dermal inflammation the liposome-entrapped compound is selected from the group consisting of steroidal antiinflammatory agents, non-steroidal antiinflammatory agents, methotrexate, azaribine, etretinate, anthralin, psoralins, and immunosuppressants such as cyclosporine.

Brief Summary Paragraph Right (64):
The invention also includes, in yet another related aspect, a method of preparing an anti-inflammatory agent for localization in an inflamed dermal region, after parenteral injection. The method includes entrapping the agent in liposomes which are characterized by: (a) composed of vesicle-forming lipids including an amphipathic vesicle-forming lipid derivatized with a hydrophilic biocompatible polymer of a size and in a molar amount effective to extend liposome blood circulation time, measured 24 hours after injection of the composition, severalfold and over that achievable in the absence of the hydrophilic polymer, (b) liposomes having a selected mean particle diameter in the size range between about 0.07-0.20 microns, (c) containing in liposome-entrapped form, an antiinflammatory agent effective against the source of the inflammation, and (d) ability to accumulate selectively in the inflamed tissue following parenteral administration, thereby to concentrate liposome-entrapped agent at the site of inflammation.

Brief Summary Paragraph Right (67):
In still another preferred embodiment, the liposome-entrapped antiinflammatory agent is a steroidal antiinflammatory compound. In a related embodiment, the antiinflammatory agent is selected from the group consisting of prednisone, methylprednisolone, paramethazone, 11-fludrocortisol, triamcinolone, betamethasone, dexamethasone, and beclomethasone.

Brief Summary Paragraph Right (68):
In another preferred embodiment, the preparation method is used to produce a liposomal preparation for inflammation associated with psoriasis, and the liposome-entrapped antiinflammatory agent is selected from the group consisting of steroidal anti-inflammatory agents, non-steroidal antiinflammatory agents, methotrexate, azaribine, etretinate, anthralin, psoralins, and immunosuppressants such as cyclosporine.

Detailed Description Paragraph Right (30):
Passive loading by entrapment is employed for certain markers, as described in Example 4, and for certain antiinflammatory agents, particularly those which are therapeutically active at relatively low drug doses, and/or which are highly soluble in aqueous solutions. Here the drug is either dissolved in the aqueous phase used to hydrate the lipid or included with the lipids in liposome formation process, depending on the solubility of the compound.

Detailed Description Paragraph Right (32):
One class of antiinflammatory agents useful in the invention described herein, the antiinflammatory corticosteroids, are characterized by a high degree of lipophilicity. Another useful antiinflammatory agent, cyclosporine, similarly is

highly lipophilic. The concentration of hydrophobic drug which can be accommodated in the liposomes will depend on drug/lipid interactions in the membrane, but is generally limited to a drug concentration of less than about 20 .mu.g drug/mg lipid. It has been found that for certain hydrophobic drugs, the highest concentration of encapsulated material which can be achieved by passive loading is limited by their low intrinsic water solubility. It has also been found that liposomal trapping and delivery of certain antiinflammatory steroids is enhanced by inclusion of a relatively high concentration (greater than 50 mole percent) of cholesterol in the liposome composition, as described in co-pending, co-owned, and allowed U.S. patent application Ser. No. 07/444,360, filed Dec. 1, 1989, now U.S. Pat. No. 5,192,528 and co-owned U.S. Pat. Nos. 5,049,389 and 5,043,165, all of which are incorporated herein by reference.

Detailed Description Paragraph Right (60):
A number of inflammatory diseases and allergic reactions may be treated systemically with steroidal antiinflammatory agents; however due to the undesirable side effects of such agents, their prolonged use is generally reserved for particularly severe afflictions. Administration of systemic steroids is indicated for urticaria resulting from an undesirable immune reaction, multiple sclerosis, and organ implant. It is appreciated that these states can be advantageously be treated with liposome-entrapped steroidal compounds, and that such treatment is anticipated to reduce overall the dose of drug administered to the whole body and thereby to reduce unwanted side effects attributable to such drugs. Additionally, as discussed below, by reducing such systemic side effects, the method of the invention makes feasible treatment of diseases or conditions in which use of steroids was previously considered unwarranted or unadvisable, due to the relative severity of the state, relative to the side effects, and/or the length of treatment required. For example, long term use of adrenocorticosteroids for treatment of less severe cases of inflammation, such as for eczematous dermatitis, although considered beneficial, is not generally recommended, due to the side effects inherent in such systemic treatment regimens. Side effects associated with long term systemic adrenocorticosteroid usage include suppression of the hypothalamic-pituitary-adrenal axis (Cushing's syndrome), fluid and electrolyte disturbances, hypertension, peptic ulceration, osteoporosis, and myopathy.

Detailed Description Paragraph Right (61):
Other agents generally useful in the treatment of inflammation include, but are not limited to free radical scavenging agents such as superoxide dismutase and nonsteroidal antiinflammatory drugs (NSAIDs), including, but not limited to salicylates (exemplified by aspirin), pyrazolon derivatives (exemplified by phenylbutazone), indomethacin, sulindac, tolmetin, fenamates (exemplified by meclofenamate), proprionic acid derivatives (exemplified by ibuprofen), oxicam derivatives (exemplified by piroxicam), phenylacetic acid derivatives (exemplified by diclofenac), etodolac, and nabumetone. Generally, although many of these drugs possess excellent antiinflammatory properties, side effects limit their use at doses effective to provide effective antiinflammatory treatment. In accordance with the invention, formulations of such drugs in liposomes having enhanced circulation times will are contemplated to provide selective relief of inflammation in subjects requiring such treatment. Other exemplary antiinflammatory agents are discussed with respect to specific indications, below.

Detailed Description Paragraph Right (64):
As described above, the liposomal compositions and treatment methods can be used to concentrate compounds to psoriatic lesions. In humans, psoriasis is a chronic condition which, although not life-threatening, can be debilitating. The precise cause of the disorder is unknown, though it has been suggested that neurogenic factors, including neuropeptides, are involved in its etiology (Pincelli). A number of therapeutic agents, including steroidal and non-steroidal antiinflammatory agents, antiproliferative agents (methotrexate, azaribine), immunosuppressants such as cyclosporine, and miscellaneous agents, such as etretinate, anthralin, psoralins and coal tar, are currently used in treatment of psoriasis. As described in Section III, above, liposomal compositions made in accordance with the invention are effective to localize and concentrate in psoriatic lesions. It is contemplated that similar liposomes, having entrapped antipsoriasis agents will be useful in treatment of psoriasis and other dermatological lesions.

CLAIMS:

5. The method of claim 1, wherein the dermal inflammation is a psoriatic dermal inflammation, and the liposome-entrapped compound is selected from the group consisting of steroidal antiinflammatory agents, nonsteroidal antiinflammatory agents, immunosuppressant agents, methotrexate, azaribine, etretinate, anthralin, and psoralins.

L7: Entry 9 of 36 File: USPT Nov 10, 1998

DOCUMENT-IDENTIFIER: US 5834511 A
TITLE: DL- DI- or tri-hydroxyphenylglycine alkyl esters for the treatment of inflammatory and allergic conditions

Brief Summary Paragraph Right (14):
Galenic formulations comprising the compounds of formula (1) will be understood as meaning in particular emulsions, ointments, gels, sprays, powders and the like. Compounds of formula (1) may also be contained in liposomes or used in pharmacological compositions with conventional carriers and penetration enhancers, for example urea, propylene glycol, oleic acid and the like [q.v. also Barry, B. W. in: Schroot,B.; Schaefer,H. (Eds.): Pharmacol. Skin., Vol.1, pp.121, Karger, Basel 1987]. The pharmaceutical composition will usually contain the compounds of formula (1) in amounts of 0.01 to 15% by weight, preferably of 0.1 to 5% by weight, of the total mixture. For the treatment of the conditions listed hereinabove, the pharmaceutical composition of this invention may contain, in addition to the compounds of formula (1), further pharmaceutical agents having antiphlogistic activity, typically including antiinflammatory agents, antipsoriatic agents, cell proliferation regulators, and antiallergic, gastroprotective and antiasthmatic agents.

WEST Search History

DATE: Wednesday, April 17, 2002

Set Name side by side	Query	Hit Count	Set Name result set
DB=USPT,JPAB,EPAB,DWPI,TDBD; PLUR=YES; OP=OR			
L7	liposome$ same (antiinflammatory adj1 agent$)	36	L7
L6	liposome$ same (antiinflammatory)	89	L6
L5	liposome$ same (free adj5 antiinflammatory)	1	L5
L4	liposome$ same (free adj1 antiinflammatory)	0	L4
L3	liposome$ same (free adj1 antiinflammaorty)	0	L3
L2	liposome$ same (free adj1 drug)	206	L2
L1	liposome$ same (drug adj1 outside)	2	L1

END OF SEARCH HISTORY